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Development of a clinical decision rule for the early safe discharge of patients with mild traumatic brain injury and findings on CT brain scan: a retrospective cohort study.

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Abstract

International guidelines recommend routine hospital admission for all patients with mild traumatic brain injury (TBI) who have injuries on CT brain scan. Only a small proportion of these patients require neurosurgical or critical care intervention. We aimed to develop an accurate clinical decision rule to identify low risk patients safe for discharge from the emergency department (ED) and facilitate earlier referral of those requiring intervention.

A retrospective cohort study of case-notes of patients admitted with initial GCS13-15 and injuries identified by CT was completed. Data on a primary outcome measure of clinically important deterioration (indicating need for hospital admission) and secondary outcome of neurosurgery, ICU admission or intubation (indicating need for neurosurgical admission) were collected. Multivariable logistic regression was used to derive models and a risk score predicting deterioration using routinely reported clinical and radiological candidate variables identified in a systematic review. We compared the performance of this new risk score with the Brain Injury Guideline (BIG) criteria, derived in the USA.

1699 patients were included from 3 English Major Trauma Centres. 27.7% (95% CI: 25.5% to 29.9%) met the primary, and 13.1% (95% CI: 11.6% to 14.8%) met the secondary, outcome of deterioration. The derived clinical decision rule suggests that patients with simple skull fractures or intracranial bleeding less than 5mm in diameter who are fully conscious could be safely discharged from the Emergency Department. The decision rule achieved a sensitivity of 99.5% (95% CI: 98.1% to 99.9%) and specificity of 7.4% (95% CI: 6% to 9.1%) to the primary outcome. The BIG criteria achieved the same sensitivity but lower specificity (5%).

Our empirical models showed good predictive performance and outperformed the BIG criteria. This would potentially allow ED discharge of one in twenty patients currently admitted for observation. However prospective external validation and economic evaluation is required.

Key Words:

Mild Traumatic Brain Injury; Prognostic modelling; Intra-cranial haemorrhage; Minor Head Injury.

Background

Over 1.4 million patients annually attend Emergency Departments (EDs) in the UK following head trauma of which ninety-five percent have a normal or mildly impaired conscious level at presentation - Glasgow Coma Scale (GCS) score of 13-15.[1] The majority of Emergency Department Computed Tomography (CT) scans for diagnosing Traumatic Brain Injury (TBI) are conducted in these patients with apparently mild injury. In this group the prevalence of brain injuries, skull fractures and intracranial bleeding is 7%, whilst only 1% of CT scans identify life-threatening TBI.[2]

The management of patients with mild TBI and injuries identified by CT imaging is controversial. Some centres advocate that all patients should be admitted under specialist neurosurgical care and undergo repeat CT imaging.[3, 4] The Brain Injury Guideline criteria (BIG), a consensus derived risk tool currently used in some centres in the USA, advocate the discharge of selected GCS 13-15 patients from the ED with injuries on CT (Supplementary Material 1).[5] We recently published a systematic review of predictors of deterioration in this

cohort identifying some single factors associated with deterioration, but there was no good empirical evidence to guide post imaging management in this group[4].

In England national (National Institute of Health and Clinical Excellence - NICE) head injury guidelines recommend that patients with TBI identified by CT are admitted to hospital.[1] However, they do not define which injuries are clinically significant and which patients benefit from specialist neurosurgical care. Other guidelines used internationally also recommend routine hospital admission for this group.[4]

There has been a paucity of research to inform the admission and referral decisions for these TBI patients with apparently mild injuries but abnormalities on CT scan.[6] Prediction modelling may help identify low risk patients who could be safely discharged from the ED. Modelling may also facilitate earlier identification of patients requiring neurosurgical intervention.

The study aims were to:

I. Estimate the prevalence of clinically important deterioration in GCS13–15 patients with traumatic CT abnormalities.
II. Develop prediction models for patient deterioration that could be used to triage hospital admission and specialist referral.
III. Compare the performance of an empirically derived prediction model with the BIG criteria.

Methods

Study Design

We conducted a retrospective cohort study using case note review of TBI patients presenting to the ED between 2010-2017 at three Major Trauma Centres in England: Hull University Teaching Hospital NHS Trust, Salford Royal NHS Foundation Trust and Addenbrooke's Hospital (Cambridge University Hospitals NHS Foundation Trust). A detailed study protocol has previously been published.[6] The study was conducted and is reported in accordance with international guidelines for prognostic research.[7]

Study Population

Population selection

Within each study centre ED, CT brain scan requests and reports were screened to identify patients with traumatic findings presenting between 2010-17. Patients were matched to case records and if meeting the inclusion criteria data were extracted on patient deterioration outcomes and candidate predictors (see below).

Inclusion Criteria

Patients aged ≥16 with a presenting GCS 13-15 who attended the ED following acute head trauma and had injuries reported on CT brain scan. The latter was defined as: skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intra-cerebral haemorrhage, contusions, subarachnoid haemorrhage and intra-ventricular haemorrhage. Intra-cerebral, intra-ventricular and subarachnoid haemorrhages were considered traumatic in aetiology when a mechanism of injury or injuries indicating trauma were recorded.

Exclusion Criteria

Patients were excluded where: a non-traumatic cause of intra-cranial haemorrhage was indicated, pre-existing CT abnormality prevented determining whether acute injury had occurred and patients transferred from other hospitals.

Outcomes

Primary Outcome

Deterioration up to 30 days following ED attendance was used which was a composite including: death attributable to TBI, neurosurgery, seizure, a drop in GCS>1, ICU admission for TBI, intubation or hospital readmission for TBI. Where reason for death, ICU admission or readmission was unknown it was attributed to TBI deterioration.

Secondary Outcome

A composite measure indicating need for neurosurgical specialist admission was used including: neurosurgery, ICU admission for TBI or intubation up to 30 days following ED attendance.

Predictors

Pre-injury anticoagulant and antiplatelet therapy were combined in a variable with two categories: i) no therapy and ii) use of either or both medications (exploratory multivariable modelling indicated they had similar effect sizes). Comorbidity was measured using the trauma modified Charlson comorbidity index. [8] Rockwood frailty scale scores were assigned to patients over 50 years using information in the case notes and data collapsed into established categories.[9, 10]

Supplementary Material 2 outlines how injuries described in written CT reports were categorised. Injury~~ies~~ severity was ~~were~~ coded using the abbreviated injury scale (AIS), injury size and presence of midline shift or mass effect. AIS codes were mapped to the Marshall classification using the method described by Lesko et al and the description of midline shift.[11] An additional category of severity of up to 2 injuries with a combined maximal diameter less than 5 mm was added. TBI severity, as measured by the Marshall classification,[11] was assessed for inclusion in the final model alongside type of haemorrhage, contusion or skull fracture present and the total number of injuries. This allowed the independent predictive value of each of these components of the CT scan to be simultaneously assessed.

Sample Size

A sample size requirement of 2000 patients was calculated using an estimated prevalence of deterioration of 10%.[6] Interim analysis found the actual prevalence of deterioration to be around 25%. Therefore the target was revised to 1700 patients, equating to 425 events and allowing 42 candidate factors to be assessed on the basis of 10 events per factor.[12]

Statistical analysis

Model Selection

The primary and secondary outcomes of deterioration were modelled as binary variables using logistic regression.[13] We used stepwise selection to find the smallest number of candidate explanatory variables that accurately predict deterioration. Table 2 summarises how candidate variables were included in modelling. For each candidate predictor an unadjusted odds ratio was calculated.

The extent of missing data on each candidate variable is shown in Table 1. Where medication use was undocumented it was taken to indicate no pre-injury use. For other variables we assumed missing data occurred at random. 25 imputed data sets were created (based on missing data in around 25% of cases) using chained equations including all candidate variables and outcomes in the ICE STATA package.[14] The midiagplots STATA function was used to compare the distributions of observed and imputed data.[15] Where continuous variables were non-normally distributed and implausible imputed values were generated, predictive mean matching was used.[14]

Model selection was performed using multivariable backward elimination with a statistical significance threshold of 0.1. All candidate predictors were initially included and imputed data sets combined using Rubin's rules at each stage of model selection. For candidate continuous variables, rather than assume a linear relationships, the best predictive form was explored with the MFPMI function using backward elimination for fractional polynomial functions in multivariable modelling.[16 17] Fractional polynomials were limited to 2 degrees of freedom when predicting the secondary outcome.

Model performance

Model fit was assessed using the Briers score averaged across imputed data sets.[18] A score of 0 implies perfect prediction and 0.25 no predictive value.

Model discrimination (how well patients with and without deterioration were distinguished) was assessed by the C-statistic, measured by combing estimates across imputed data sets using Rubin's rules.[17, 19]

Calibration measures how well predictions made by models match observations.[13] The calibration slope of selected predictors was calculated in each imputed data set and averaged.

Sensitivity analysis

Model selection and evaluation of model performance was repeated in patients with complete data.

Internal validation

Models tend to perform better on data from which they are derived (overfitting).[13] Bootstrap internal validation with 100 bootstrap samples was performed in each imputed data set to calculate the average optimism. Model selection was repeated in each bootstrap sample and performance of models selected was subtracted by performance in the original data set.[20, 21] The pooled average difference in the calibration slope between the bootstrap samples and original data was averaged across imputed data sets. This was subtracted from the original averaged calibration slope to estimate the shrinkage factor. The shrinkage factor was applied to the derived model coefficients to adjust for optimism.[13] The C statistic was adjusted for optimism using the same method.

Mild TBI Risk score development and comparison to the BIG criteria

To use our prognostic model for making to clinical decisions we derived a risk score using optimism adjusted coefficients.[22] To make the risk score clinically interpretable coefficients were standardised and rounded.[22] Individual patient risk scores were calculated. A risk score for ED discharge was proposed based on the trade-off between risk of deterioration in a discharged patient and number of patients admitted for observation.

Sensitivity and specificity of the proposed discharge score and of the BIG criteria to deterioration were calculated and compared in patients with complete data for both criteria.

Ethics

NHS Research Ethics Committee Approval was granted by West of Scotland REC 4 reference: 17/WS/0204. As a retrospective case review conducted by members of the direct care team, consent was not requited.

Results

Study population

Figure 1 summarises study population selection and Table 1 population characteristics and candidate variables. The cohort was mostly male, with around half of patients aged over 60 and quarter with either pre-injury anti-coagulant or anti-platelet use. 470 patients (27.7%; 95% CI: 25.5% to 29.9%) clinically deteriorated as defined by the primary outcome. 223 patients (13.1%; 95% CI: 11.6% to 14.8%) underwent neurosurgery, were admitted to ICU or were intubated (secondary outcome). 72 patients had deaths attributable to TBI. 471 patients had data missing from at least one candidate variable.

Model selection

Table 2 summarises the univariable associations between candidate variables and the primary outcome. Supplementary material 3 presents the distributions of imputed data.

The equivalent of 41 candidate factors were assessed in multivariable modelling to predict patient deterioration and 34 factors were assessed in modelling to predict need for

neurosurgical referral. The selected model predicting the primary outcome is presented in Table 2 and the secondary outcome in Table 3. Supplementary Material 4 presents a complete case sensitivity analysis.

Model Performance

Table 4 summarises measures of model performance. The models predicting the primary and secondary outcomes had Briers scores of 0.16 and 0.09 respectively. The model predicting composite deterioration (primary outcome) had an optimism-adjusted C-statistic of 0.75 and the model predicting need for specialist neurosurgical admission had an optimism-adjusted C-statistic of 0.85. The trade-off between the sensitivity and specificity of these models is shown in the ROC curves in Supplementary Material 5.

The mild TBI Risk Score

Table 5 presents the weighted risk score derived from our prognostic model predicting deterioration. Haemoglobin, although a statistically significant predictor in multivariable modelling was not included as, due to the small effect size and range of abnormal values, inclusion did not improve performance (Supplementary Material 6). Based on the trade-off between sensitivity and specificity, a patient risk score of 0 was used as a threshold for ED discharge. Patients as this cut off had the following characteristics: initial GCS15, single simple skull fracture or haemorrhage<5mm, up to 2 extra-cranial bony or organ injuries not requiring hospital admission, not anticoagulated/taking antiplatelets, no cerebellar/brain stem injuries, and normal neurological examination (Table 5). Patients with a risk score of 1-5 had a 17.5% risk of deterioration and patients with a risk score >5 had 54% risk of deterioration (Supplementary material 7)

The performance of the BIG criteria and our risk score were assessed in the 1569 patients with complete data for both classification systems. A threshold of 0 in our risk score achieved a sensitivity of 99.5% (95% CI: 98.1% to 99.9%) and specificity of 7.4% (95% CI: 6% to 9.1%) to the primary outcome. The BIG criteria for discharge achieved the same sensitivity for deterioration but lower specificity (Table 6). Table 6 summarises the characteristics of the false negatives (patients meeting the discharge threshold who deteriorated) in both approaches. No patients recommended for discharge by either criteria, died or required neurosurgery, but 1 patient recommended for discharge by the BIG criteria required intubation. The BIG criteria would have allowed discharge of 57 patients (3.6%) compared to 87 patients (5.5%) with our risk score.

Discussion

Summary

To our knowledge, this is the first UK study to report the risk of deterioration in all initial mild TBI patients with traumatic injuries reported on CT brain scan and study internationally to develop a prognostic model and risk tool for avoiding unnecessary hospital admissions. We also report the first independent validation of the BIG criteria.

The estimated prevalence of deterioration was 27.7%. Our prognostic models for composite measures of deterioration had optimism adjusted C statistics of 0.75 and 0.85, indicating good discrimination between patients with and without deterioration or need for neurosurgical care.

Using our risk score, derived from the prognostic model, to hypothetically direct need for hospital admissions we identified that it would appear safe to discharge from the

Emergency Department patients who are fully conscious with no focal neurology (GCS15) – not taking anticoagulant or antiplatelet medication who have with a single simple skull fracture or haemorrhage<5mm (not cerebellar or brainstem) on CT brain scan and up to two extra-cranial bony or organ injuries not requiring hospital admission (risk score 0). This derived decision rule, achieved a sensitivity of 99.5% and specificity of 7.4% for deterioration. Categorisation of patients for discharge using the BIG criteria achieved the same sensitivity but a lower specificity.

The model predicting need for neurosurgical admission (based on risk of an interventional outcome) found higher age and frailty reduces risk. This probably reflects clinical selection of patients, with frail older patients less likely to undergo invasive interventions.

Strengths

We believe this is the largest multi-centre cohort study undertaken to estimate the prevalence of a composite measure of deterioration in this population.[4] The study was powered to develop a prognostic model predicting this outcome. Candidate predictor factors were selected a priori on the basis of existing literature.[6] We followed established techniques for handling missing data, prognostic modelling and adjusting for optimism.[7, 13, 16, 23] Unlike risk stratification systems based solely upon CT findings,[24-26] we have assessed a range of additional patient characteristics, test results and other clinical factors for deterioration for inclusion in our model so as to achieve the maximum predictive accuracy. Our risk score is the first empirically derived scoring system which can to be used to inform admission decisions in this TBI population and incorporates both patient characteristics and other clinical risk factors alongside CT findings.

Limitations

Due to the resource implications of conducting a prospective study we pragmatically chose a retrospective study design. Around 25% of patients had missing data, but as these data were mainly missing through poor recording or missing notes, and therefore missing at random, imputation techniques were valid. Documentation inaccuracies may have introduced random error but are unlikely to have introduced systematic bias.

We classified TBI severity using information in written CT reports by using AIS coding to map to a modified Marshall classification. Poor reporting of the size of injuries and extent of mass effect meant most injuries were classified as equivalent to Marshall classification II. Better systematic and standardised reporting may have allowed TBI severity to be better classified and improved the performance of the derived models. We were unable to assess whether using other scoring systems to classify TBI severity such as the Stockholm, Helsinki or NIRIS scoring systems would improve the performance of the derived model. [24-26] Unlike with the Marshall classification, there is no validated way to map between AIS coding and these classification systems. However, type of injury was considered for inclusion in the model, alongside the Marshall classification and number of injuries

Outcomes were limited to those recorded in hospital records, which may mean that patient deterioration in the community was missed. However, this is unlikely and a check in Hull of deaths recorded in patients eligible for entry on the national trauma registry (linked to office of national statistic mortality reporting) found no missed deaths.

We only assessed the predictive value of routinely collected factors. We could not assess the potential predictive value of using non-routinely collected variables identified in our review[6] or biomarkers.

Although we have internally validated our derived models, they have not been externally validated. There is debate about the best way to combine imputation of missing data and internal validation bootstrapping techniques.[21] We chose to bootstrap within imputations due to lower computational complexity. This has been shown in simulation studies to provide accurate estimates of the shrinkage factor.[21] Other studies[27] found imputing within bootstraps better adjusts for optimism and therefore despite adjusting for overfitting, our models may perform less well when applied to new data.

The lower prevalence of the secondary outcome than expected means our study may not be adequately powered to derive a model accurately predicting this outcome.

Comparison Previous literature

The estimated prevalence of clinical deterioration at 27.7% was higher than previously reported. In our review we found the pooled prevalence of clinical deterioration to be around 10% .[4] This reflects differences in study design; previous studies used narrower outcome definitions, such as neurological deterioration or ICU intervention,[4] whilst we used a wide composite primary outcome aimed at encompassing need for hospital admission. We assessed an unselected GCS13-15 population, whilst previous studies often restricted their inclusion criteria on the basis of GCS scores, injury severity, admitting inpatient specialty and medication use.[6]

Research assessing prognostic factors in this TBI population have frequently used sample sizes based on convenience and lacked the statistical power to assess potential predictors simultaneously.[4, 28] Our study was sufficiently powered to assess over 40 candidate variables in multivariable modelling. Previous research found initial GCS, type of brain injury, anti-coagulation and age were the strongest predictors of adverse outcomes in this population.[4] In our multivariable model all these factors were also found to be predictors of deterioration.

Studies evaluating the BIG criteria in the Level 1 trauma centre in the USA, where it is routinely applied, found around 10% of patients met the criteria for ED discharge and no patient that met these criteria had adverse outcomes.[5, 29] In our cohort 4% of patients met the criteria for ED discharge and two of these patients deteriorated. Our study cohort was on average older and had a lower GCS than studies previously assessing the BIG criteria, which may account for the difference in performance.

Implications

Internationally, and particularly in the USA, there is wide variation in admission practices in this group with a range of specialist admission and discharge criteria used on the basis of limited evidence.[5, 30-32] Accurate risk prediction has the potential to help rationalise admission decisions in this group. Between April 2014 and June 2015 around 11, 000 TBI patients were admitted to specialist neurosurgical centres in the UK and over 50% of these patients had mTBI.[33] Currently all patients with TBI identified by CT imaging are admitted to hospital. ~~Consequently, any risk stratification tool which could safely reduce unnecessary admissions may save significant health service resources.~~Therefore, despite the low specificity of our model and the high false positive rate, application of our model could

improve clinical care by reducing unnecessary hospital admissions and thereby save health service resources and reduce patient inconvenience. ~~Internationally, and particularly in the USA, there is wide variation in admission practices in this group with a range of specialist admission and discharge criteria used on the basis of limited evidence.[5, 30-32] Accurate risk prediction has the potential to help rationalise admission decisions in this group.~~

Our risk tool demonstrated good predictive ~~accuracy (99.5%~~ sensitivity (99.5%) to our primary outcome~~)~~ at the proposed threshold for ED discharge. This would have allowed the discharge of 87/1569 patients (5.5%). At this sensitivity a negative predictive value of 97.7% was achieved (about a 1 in 50 chance of a discharged patient deteriorating). This may not be clinically acceptable, but no patient recommended by our risk score for discharge died, required neurosurgery or an ICU intervention. One patient recommended for discharge had a report indicating a possible second lesion, and therefore may have been admitted in clinical practice. The BIG criteria achieved the same sensitivity (99.5%) to the primary outcome but its lower specificity means clinical application would result in fewer patients being discharged.

The high predictive accuracy of our model for the secondary outcome (AUC = 0.85) suggests it could be used to triage neurosurgical admissions in this population. The acceptable level of risk of requiring invasive intervention for a patient admitted under a non-specialist team is unknown and is likely to vary between centres. The lower prevalence of this outcome means the estimated model may be less accurate and we regard this as a starting point for further research.

Both our prognostic model and the BIG criteria should be validated prospectively before they could be used in clinical practice. A prospective study design would address the

weaknesses in outcome collection highlighted earlier, including assessing the predictive value of CT severity classification systems other than the Marshall classification system, and allow the inclusion of non-routinely collected prognostic factors including biomarkers. Improved systematic reporting of CT scans could possibly increase the predictive accuracy of our model and further increase the performance of our risk tool.[25, 34] Economic evaluation is also required to comprehensively assess the implication for both patient outcomes and resource use of using the model.

Conclusion

This is the first study to empirically derive a prognostic model for patients with mTBI and injuries identified by CT imaging and independently validate the BIG criteria. Our empirically derived risk tool performed better than the BIG criteria and could be used to safely discharge from the ED one in twenty patients currently routinely admitted for observation. Both our prognostic model and the BIG criteria now require prospective external validation and economic evaluation.

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No competing financial interests exist.

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Authors' contributions:

The idea for the study was conceived by Carl Marincowitz with help from Trevor Sheldon, Fiona Lecky and Victoria Allgar. Hadir Elbeltagi, Faye Johnson and Eimhear Quinn completed data collection at Salford Royal Hospital. Silvia Tarantino completed data collection at Addenbrooke's Hospital. Carl Marincowitz completed data collection at Hull Royal Infirmary. The analysis was completed by Carl Marincowitz with specialist advice regarding research methods and prognostic modelling from Trevor Sheldon, Victoria Allgar and Fiona Lecky. Fiona Lecky, Angelos Kolias, Peter Hutchinson and Will Townend provided specialist advice

regarding the clinical context and application of the research. All authors read and approved the final manuscript.

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Table 1: Characteristics of the study population

Table 2: Candidate factors' (uni and multi-variable) associations with the outcome of deterioration

Table 3: Candidate factors' (uni and multi-variable) association with neurosurgical admission

Table 4: Performance of predictive models

Table 5:Mild TBI Risk score

Table 6: Performance of mTBI risk score and BIG criteria

Table 1: Characteristics of the study population

Candidate Factor	Category	Mean (SD), min-max OR N (%)	Missing data N=1699
Age	Years	58.2 (SD 23.3) 16-101 Age≥65 = 44.9%	None
Sex	Male Female	67% (Median Age= 52) 33% (Median Age= 69)	None
GCS	15 14 13	976 (58%) 533 (31%) 185 (11%)	5 (0.3%)
Mechanism of Injury	Assault Fall Fall from height RTC Sport Other	228 (13%) 1090 (64%) 361 (21%) 298 (18%) 21 (1%) 30 (2%)	31 (1.8%)
Intoxicated	Yes	494 (29%)	38 (2.2%)
Seizure pre-hospital or in ED	Yes	74 (4%)	10 (0.6%)
Vomit pre-hospital or in ED	Yes	310 (18%)	12 (0.7%)
Preinjury Anti-coagulation or anti-platelets	Anticoagulation use Antiplatelet use Both	155 (9%) 294 (17.3%) 8 (0.5%)	None

Abnormal First Neurological Examination	Yes	233 (14.5%)	89 (5.2%)
Initial Blood pressure	Mean Arterial Pressure mmHG	98.5 (SD 17) 43-193	61 (3.6%)
Initial Oxygen Saturation	%	97.4 (SD 2.4) 80-100	59 (3.5%)
Initial Respiratory Rate	RR per Min	17.9 (SD 3.5) 10-48	94 (5.5%)
Haemoglobin	Grams/litre	136 (SD 19.1) 68-265	211 (12.4%)
Platelet Value	10^9/L	232 (SD 77) 2-742	211 (12.4%)
Number of Injuries on CT	1 2 3 4 5 Multiple diffuse injury*	824 (48.5%) 400 (23.6%) 217 (12.7%) 142 (8.4%) 103 (6.1%) 13 (0.8%)	None
Injury severity on CT (~~Modified~~ Based on the Marshall Classification system and described in detail supplementary Material 2)	**1)** Simple Skull Fractures **2)** Complex Skull fractures **3)**1-2 bleeds < 5mm (total) **4)** No or minimal mass effect **5)** Significant midline shift	66 (3.9%) 123 (7.2%) 208 (12.2%) 1001 (58.9%) 159 (9.4%) 122 (7.2%) 22 (1.2%)	None

	6) High/mixed-density lesion** **7)** Cerebellar/Brain stem injury		
Skull Fracture (simple)	Yes	316 (19%)	None
Skull Fracture (complex)	Yes	360 (21%)	None
Contusion	Yes	580 (34%)	None
Extradural bleed	Yes	135 (8%)	None
Intraparenchymal haemorrhage	Yes	240 (14%)	None
Subdural bleed	Yes	694 (41%)	None
Intra-ventricular bleed	Yes	50 (3%)	None
Subarachnoid bleed	Yes	536 (32%)	None
Rockwood Clinical Frailty Scale (CFS)	Patients under 50 CFS 1-3 CFS 4-6 CFS 6-9	649 (39%) 642 (38%) 308 (18.5%) 72 (4.5%)	28 (1.6%) cases
Comorbidity	Charlson Index	1.4 (SD 2.9) 0-28 (range)	20 (1.2%) cases
ISS	Body regions excluding head	5.2 (SD 5.2) 0-75 (range)	None

*diffuse injuries refer to multiple tiny intracerebral haemorrhages/contusions/diffuse axonal injuries

**This category corresponds to Marshall Classification VI (volume>25mls) and corresponds to a need for surgical evacuation by the Marshall Classification.

Table 2: Candidate factors' (uni and multi-variable) associations with the outcome of deterioration

Candidate Factor	Category	Univariable effect on risk of deterioration : Odds ratio (95% CI)	Multivariable effect on risk of deterioration: Odds Ratio (95% CI)
GCS Vs 15	GCS14 GCS13	1.8 (1.4 to 2.3) 3.1 (2.3 to 4.4)	1.6 (1.2 to 2.1) 2.3 (1.6 to 3.3)
Preinjury Anti-coagulation or anti-platelets	Yes	1.7 (1.3 to 2.1)	1.4 (1.03 to 1.8)
Abnormal Neurological Examination	Abnormal	2.3 (1.7 to 3)	1.7 (1.2 to 2.3)
Haemoglobin	Grams/litre (1 unit increase)	0.99 (0.98 to 0.99)	0.99 (0.98 to 1)
Number of Injuries on CT Vs 1	2 3 4 5 Diffuse injury	1.4 (1.1 to 1.9) 1.8 (1.3 to 2.5) 3.2 (2.2 to 4.7) 3.7 (2.5 to 5.7) 1.1 (0.3 to 4.2)	1.3 (0.97 to 1.8) 1.6 (1.1 to 2.3) 2.5 (1.6 to 3.8) 2.8 (1.7 to 4.6) 1.4 (0.3 to 5.3)
Injury severity on CT Vs simple skull fracture (categories described in detail supplementary material 2)	2) Complex Skull fractures 3)1-2 bleeds < 5mm (total) 4) No or minimal mass effect 5) Significant midline shift 6) High/mixed-density lesion 7) Cerebellar/Brain stem injury	1.4 (0.5 to 4.2) 1.4 (0.5 to 3.8) 4 (1.6 to 10) 13.7 (5.2 to 35.8) 40.1 (15 to 111.9) 8.1 (2.3 to 29.2)	1.4 (0.5 to 4.3) 1.1 (0.4 to 3.1) 2.3 (0.9 to 5.9) 6.8 (2.5 to 18.5) 21.6 (7.7 to 60.7) 7 (1.9 to 25.7)
Extracranial Injury	ISS 1 unit increase	1.02 (1.00 to 1.04)	1.03 (1.002 to 1.05)
Age	Year 1 unit increase	1.01 (1.006 to 1.015)	*
Sex	Female	1.04 (0.83 to 1.31)	*
Intoxicated	Yes	0.98 (0.77 to 1.24)	*

Seizure pre-hospital or in ED	Yes	1.2 (0.7 to 2)	*
Vomit pre-hospital or in ED	Yes	1.3 (1 to 1.7)	*
Initial Blood pressure	1 unit increase, Mean Arterial Pressure mmHG	1.004 (1 to 1.01)	*
Initial Oxygen Saturation	% (1 unit increase)	0.99 (0.95 to 1.04)	*
Initial Respiratory Rate	RR per Min (1 unit increase)	1.05 (1.02 to 1.08)	*
Platelet Value	10^9/L (1 unit increase)	1 (0.997 to 1)	*
Skull Fracture (Simple)	Yes	1.1 (0.8 to 1.4)	*
Skull Fracture (Complex)	Yes	0.955 (0.7 to 1.2)	*
Contusion Present	Yes	1.4 (1.1 to 1.7)	*
Extradural bleed	Yes	2 (1.4 to 2.9)	*
Intraparenchymal haemorrhage Present	Yes	1.2 (0.9 to 1.6)	*
Subdural bleed	Yes	2.2 (1.8 to 2.8)	*
Intra-ventricular bleed	Yes	1.9 (1.81to 3.4)	*
Subarachnoid bleed	Yes	1.4 (1.1 to 1.7)	*
Comorbidity	Charlson Index	1.07 (1.03 to 1.11)	*
Rockwood Frailty Score Vs under 50	CFS 1-3 CFS 4-6 CFS 7-9	1.3 (1.04 to 1.7) 1.6 (1.2 to 2.2) 2.8 (1.7 to 4.6)	*

* Not selected into model

Table 3: Candidate factors' (uni and multi-variable) association with neurosurgical admission

Candidate Factor	Category	Univariable effect on risk of deterioration : Odds ratio (95% CI)	Multivariable effect on risk of deterioration: Odds Ratio (95% CI)	
Age	Year (1 unit increase)	0.99 (0.99 to 1)	$(Age/10)^3$ Fractional Polynomial	0.997 (0.996 to 0.9989
GCS Vs 15	GCS14 GCS13	2 (1.5 to 2.8) 3.8 (2.6 to 5.7)	2.3 (1.6 to 3.3) 3.7 (2.3 to 5.9)	
Abnormal Neurological Examination	Abnormal	2.4 (1.7 to 3.4)	1.9 (1.3 to 3)	
Haemoglobin	Grams/litre (1 unit increase)	1 (0.99 to 1.01)	0.99 (0.98 to 1)	
Injury severity on CT Vs simple skull fracture (categories described in detail supplementary material 2)	2) Complex Skull fractures 3)1-2 bleeds < 5mm (total) 4) No or minimal mass effect 5) Significant midline shift 6) High/mixed-density lesion 7) Cerebellar/Brain stem injury	1.9 (0.4 to 9.6) 1 (0.2 to 4.8) 3.3 (0.8 to 13.6) 11.5 (2.7 to 49) 41.7 (9.8 to 178) 8 (1.3 to 47.6)	0.9 (0.5 to 4.9) 0.8 (0.1 to 4.1) 2.3 (0.5 to 9.7) 7.4 (1.6 to 33.9) 37.1 (8.1 to 169) 8.5 (1.3 to 56.2)	
Skull Fracture (Complex)	Yes	1.7 (1.3 to 2.3)	2 (1.3 to 3)	
Subdural bleed	Yes	2.2 (1.6 to 2.9)	1.7 (1.2 to 2.5)	
Extracranial Injury	ISS (1 unit increase)	1.03 (1.004 to 1.06)	1.06 (1.03 to 1.09)	
Rockwood Frailty Score Vs under 50	CFS 1-3 CFS 4-6 CFS 7-9	1.2 (0.9 to 1.6) 0.4 (0.2 to 0.7) 0.09 (0.01 to 0.6)	1.9 (1.1 to 3.1) 0.7 (0.3 to 1.8) 0.09 (: 0.01 to 0.7)	
Sex	Female	0.66 (0.48 to 0.91)	*	

Preinjury Anti-coagulation or anti-platelets	Yes	0.95 (0.7 to 1.3)	*
Intoxicated	Yes	1.1 (0.8 to 1.5)	*
Seizure pre-hospital or in ED	Yes	1.8 (0.99 to 3.18)	*
Vomit pre-hospital or in ED	Yes	1.5 (1.1 to 2.1)	*
Initial Blood pressure	1 unit increase, Mean Arterial Pressure mmHG	1.006 (1 to 1.01)	*
Initial Oxygen Saturation	% (1 unit increase)	1 (0.94 to 1.07)	*
Initial Respiratory Rate	RR per Min (1 unit increase)	1 (0.99 to 1.07)	*
Platelet Value	10^9/L (1 unit increase)	0.99 (0.998 to 1.001)	*
Number of Injuries on CT Vs 1	2 3 4 5 Diffuse injury	1.4 (0.98 to 2.1) 1.5 (1 to 2.4) 3.4 (2.2 to 5.3) 4.3 (2.7 to 7) 1.8 (0.4 to 8.3)	*
Skull Fracture (Simple)	Yes	1.2 (0.8 to 1.7)	*
Contusion Present	Yes	1.3 (0.997 to 1.8)	*
Extradural bleed	Yes	2.6 (1.7 to 3.9)	*
Intraparenchymal haemorrhage Present	Yes	0.7 (0.5 to 1.2)	*
Intra-ventricular bleed	Yes	0.7 (0.3 to 1.9)	*
Subarachnoid bleed	Yes	1.4 (1 to 1.9)	*
Comorbidity	Charlson Index (1 unit increase)	0.94 (0.89 to 1)	*

*Not Selected into model

Table 4: Performance of predictive models

Outcome	Measure	Apparent Performance	Average Optimism	Optimism Adjusted
Clinical Deterioration	Brier Score	0.16		
	Calibration Slope	1	0.14	0.86
	C-statistic	0.773	0.026	0.747
Need for specialist neurosurgical admission	Brier Score	0.09		
	Calibration Slope	1	0.04	0.96
	C-statistic	0.86	0.01	0.85

Table 5: Mild TBI Risk score

Factor	**Coefficient (optimism adjusted)**	**Risk Score Value**
Preinjury Anti-coagulation or anti-platelets	0.3	1
GCS 15 14 13	 0 (Vs) 0.4 0.7	 **GCS 15** 0 **GCS 14** 1 **GCS 13** 2
Normal first Neurological Examination	0.45	**Abnormal** 1.5
Number of Injuries on CT **1** **2** **3** **4** **5** **Diffuse**	 0 (Vs) 0.25 0.4 0.8 0.9 0.3	 **1** 0 **2** 1 **3** 1 **4** 3 **5** 3 **Diffuse** 1
Injury severity on CT* **1** simple skull fracture **2** complex Skull Fracture **3** 1-2 bleeds < 5mm **4** No or minimal mass effect	 0 (Vs) 0.3 0.08 0.7	 **1** 0 **2** 1 **3** 0 **4** 2

5 Significant midline shift **6** High/mixed-density lesion **7** Cerebellar/Brain stem injury	1.7 2.7 1.7	**5** 5 **6** 9 **7** 5
ISS (body regions excluding head)	0.2	**Up to 2 non-significant extra-cranial injuries**** 0 **Any significant extra-cranial injury or 3 or more injuries** 2
Hb	-0.01	Not included in risk score
Constant	-1.38	

*TBI severity categories are described in detail in Supplementary material 2

** Injuries exclude superficial lacerations and abrasions and a significant extra-cranial injury is defined as any injury requiring inpatient care

Table 6: Performance of mTBI risk score and BIG criteria

N=1569	**Deteriorated**	**Didn't deteriorate**	**Positive Predictive Value (PPV)** **Negative Predictive Value (NPV)**
Performance of Risk score			
Admission (Score>0)	423	1059	PPV = 28.5%
Discharge (Score=≤0)	2*	85	NPV = 97.7%
	Sensitivity= 99.5% (95% CI: 98.1% to 99.9%)	Specificity= 7.4% (95% CI: 6% to 9.1%)	
Performance of BIG criteria			
Admit (not BIG1)	423	1089	PPV = 28%
Discharge (BIG 1)	2*	55	NPV = 96.5%
	Sensitivity = 99.5% (95% CI: 98.1% to 99.9%)	Specificity= 4.8% (95% CI: 3.7% to 6.3%)	

*Patients recommended for discharge by our risk score who deteriorated:

1) 85 female, small subdural dropped GCS. Rockwood frailty score 4.

2) 56 male, small contusion (report stated possible 2nd small intra-cranial haemorrhage, only first injury included) and pre-injury seizure. Seizure during admission.

Patients triaged to discharge by BIG who deteriorated:

1) 85 female, small subdural dropped GCS. Rockwood frailty score 4.

2) 55 female, small subdural and poly trauma (ISS 10). Required intubation.

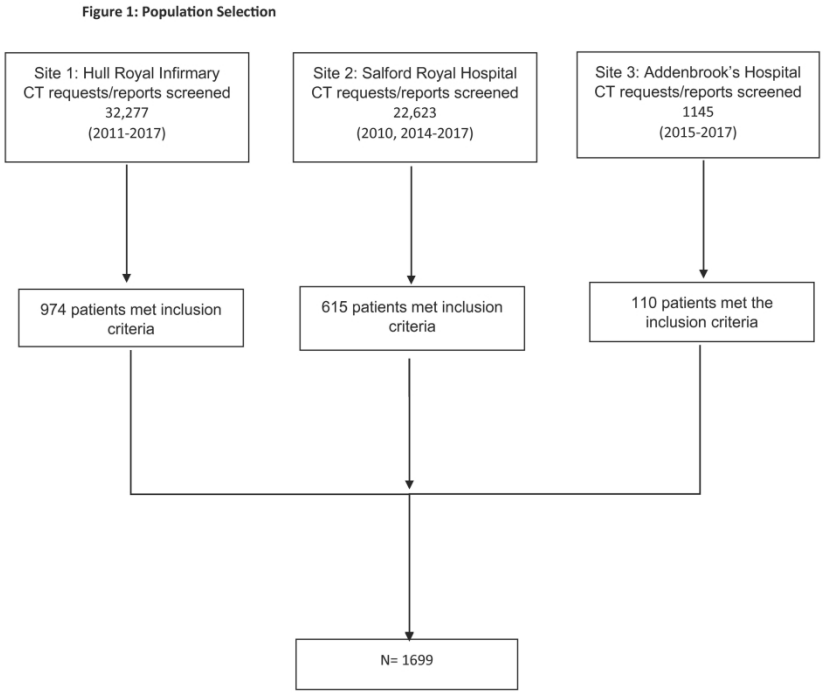


Figure 1: Population Selection

209x296mm (300 x 300 DPI)

Figure 1: Population Selection

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **Page 1**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **Page 3**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **Page 4,5**
Objectives	3	State specific objectives, including any prespecified hypotheses **Page 5**
Methods		
Study design	4	Present key elements of study design early in the paper **Page 5**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **Page 5**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up **Page 6**
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **Page 5 -10**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **Page 7 -8**
Bias	9	Describe any efforts to address potential sources of bias **Page 8-10**
Study size	10	Explain how the study size was arrived at **Page 8**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **Page 9-10**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **Page 8 -10**
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed **Page 8,9**
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses **Page 10**
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **Page 11-13**
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram **Fig 1**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **Table 1**
		(b) Indicate number of participants with missing data for each variable of interest **Table 1**
		(c) Summarise follow-up time (eg, average and total amount)

Mary Ann Liebert, Inc, 140 Huguenot Street, New Rochelle, NY 10801

Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included **Table 2 and Table 3**
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **Supplementary Material 4**
Discussion		
Key results	18	Summarise key results with reference to study objectives **Page 13**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **Page 14-15**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **Page 16-17**
Generalisability	21	Discuss the generalisability (external validity) of the study results **Page 15, 17**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **Page 18, 19**

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Supplementary Material 1: The Brain Injury Guideline (BIG) criteria:

	BIG1 (Discharge from ED after 6 hours)	BIG2 (Non-specialist hospital admission)	BIG3* (Specialist hospital admission)
Neurological Examination	GCS13-15 Normal pupils No Focal Neurological deficit	GCS13-15 Normal pupils No Focal Neurological deficit	GCS<13 Or Abnormal pupils Or Focal Neurological deficit
Intoxicated	No	No/Yes	No/Yes
Anticoagulants or Anti-platelets	No	No	Yes
Skull Fracture	No	Non-displaced	Displaced
Intracranial Bleed	Subdural Haemorrhage <5mm Or Extradural Haemorrhage <5mm Or 1 Intraparenchymal Haemorrhage <5mm Or Trace Subarachnoid Haemorrhage	Subdural Haemorrhage 5-7mm Or Extradural Haemorrhage 5-7mm Or 1-2 Intraparenchymal Haemorrhages 5-7mm Or Localised Subarachnoid Haemorrhage	All other injuries
Intra-ventricular Haemorrhage	No	No	Yes

*Patients must fulfil all the criteria of BIG1 or BIG2 to be categorised as such and are otherwise automatically in BIG3

Supplementary material 2: Categorisation of TBI severity

Category	Injury Description written CT report	AIS Codes	Equivalent Marshal Classification (Lesko et at[11])
1	Vault skull fractures	150000, 150400 150402	
2	Basal, depressed, open skull fractures	150200, 150204, 150205, 150206, 150404, 150406, 150408	I
3	1-2 Bleeds* /contusions total diameter <5mm	140605, 140631, 140639, 140651, 140693, 140694 (and written CT report indicated injury <5mm)	
4	Bleed/contusion No or minor mass effect	140602,140604,140606,140612,140614,140611,140620,140622, 140628,140629,140630,140632,140634,140638,140640,140642, 140644,140646,140650,140652,140654,140684,140688, 140686, 140699, 140676, 140678, 140680, 140682, 140799	II
5**	Bleed/contusion Significant midline shift or mass effect indicated in CT report	140202, 140660, 140662, 140664, 140666	III/IV
6	Non-evacuated mass lesion. High or mixed density mass lesion***	140608,140610,140616,140618,140624,140626,140636,140648, 140656, 140637, 140655	VI
7	Cerebellar/brainstem injury	140204,140206,140208,140210,140212,140214,140218,140299, 140402,140403,140404,140405,140406,140410,140414,140418, 140422,140426,140430,140434,140438,140442,140446,140450, 140458,140462,140466,140470,140474,140499,	VII

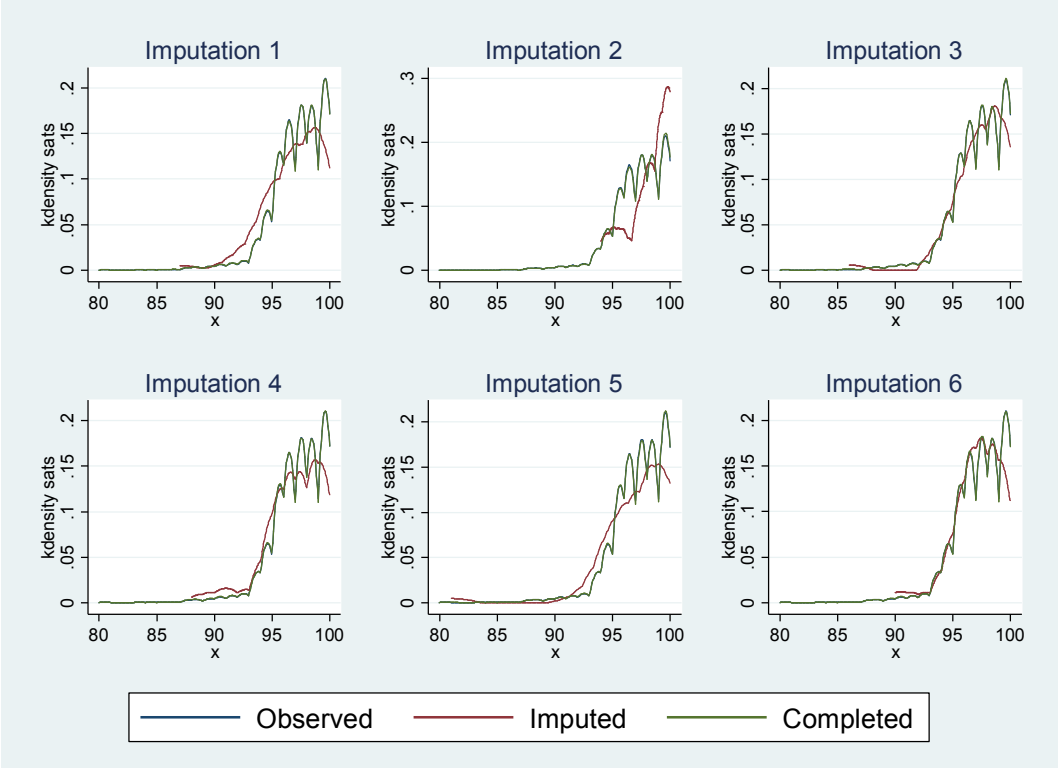
*Bleeds refers to subdural, extradural, intracerebral and subarachnoid haemorrhage

**Written CT reports did not allow easy differentiation in the extent of mass effect, and therefore Marshall III and IV categories were collapsed into 1 category.

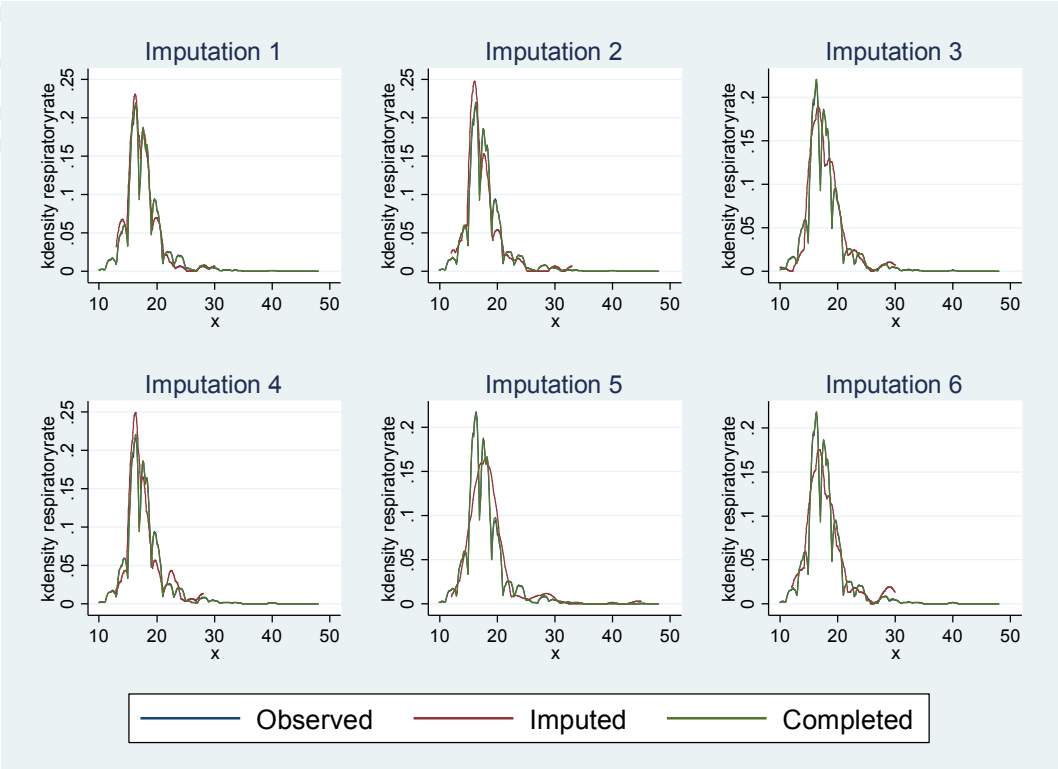
***This category refers to any lesion or combination of lesions where the mass effect is so great that the Marshall Classification recommends immediate surgical intervention.

Supplementary material 3: Distribution of observed and imputed data of first 6 imputations of 25

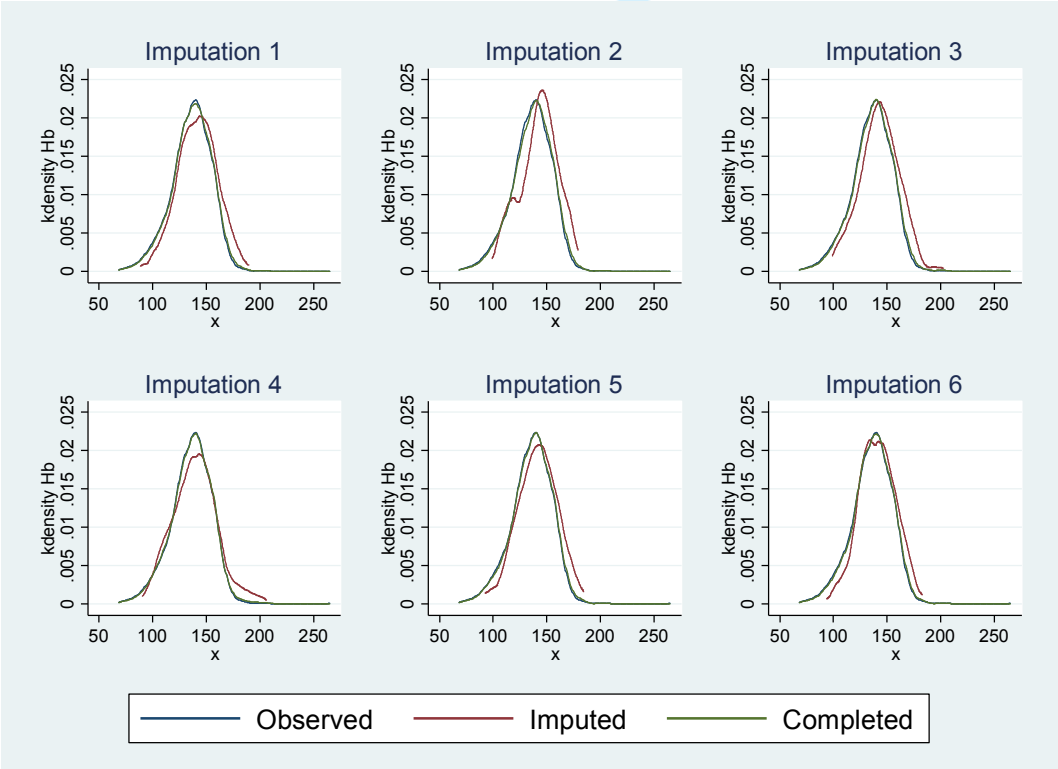
Saturations:



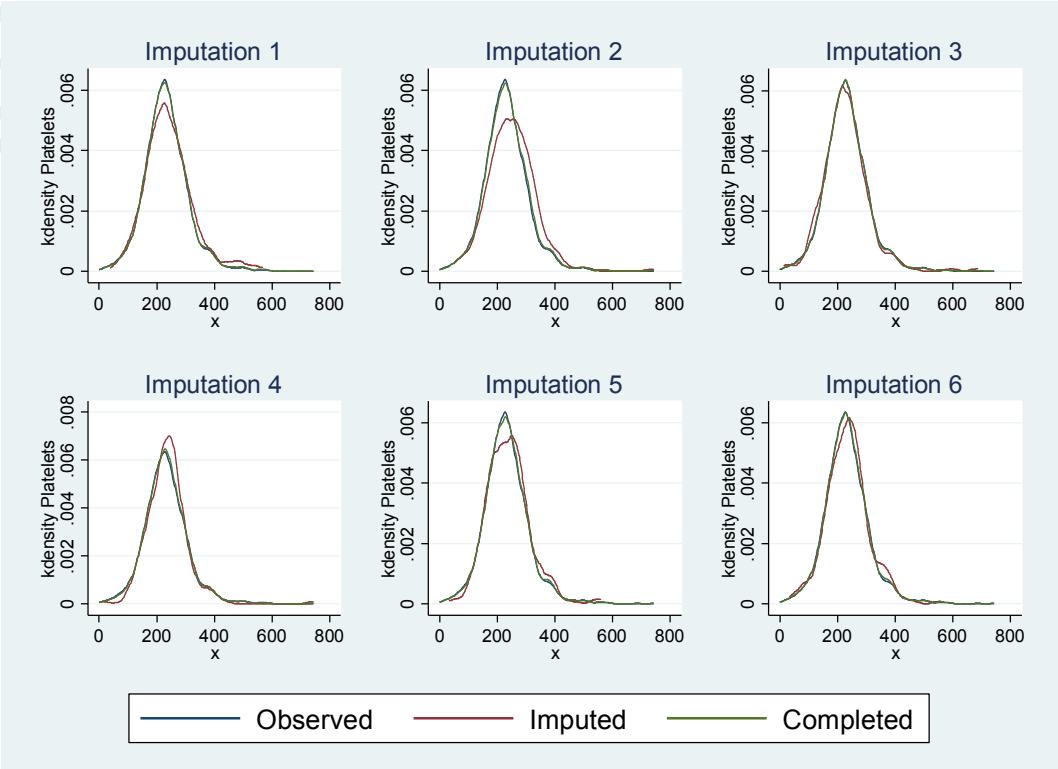
Respiratory Rate:



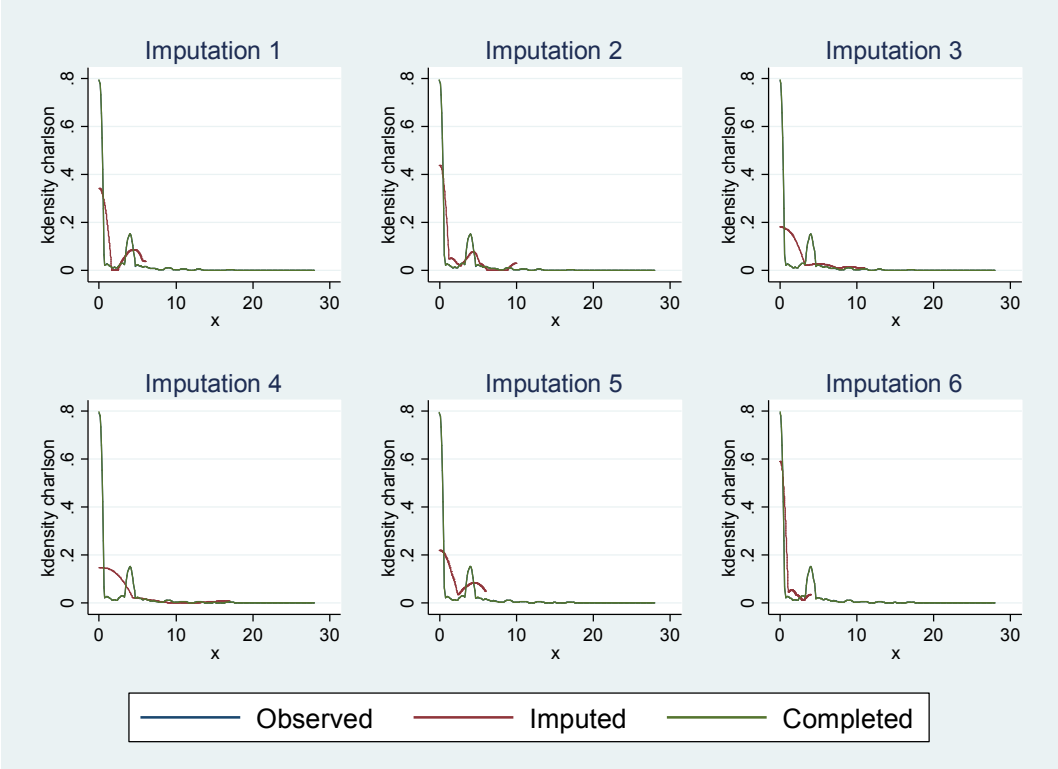
Hb:



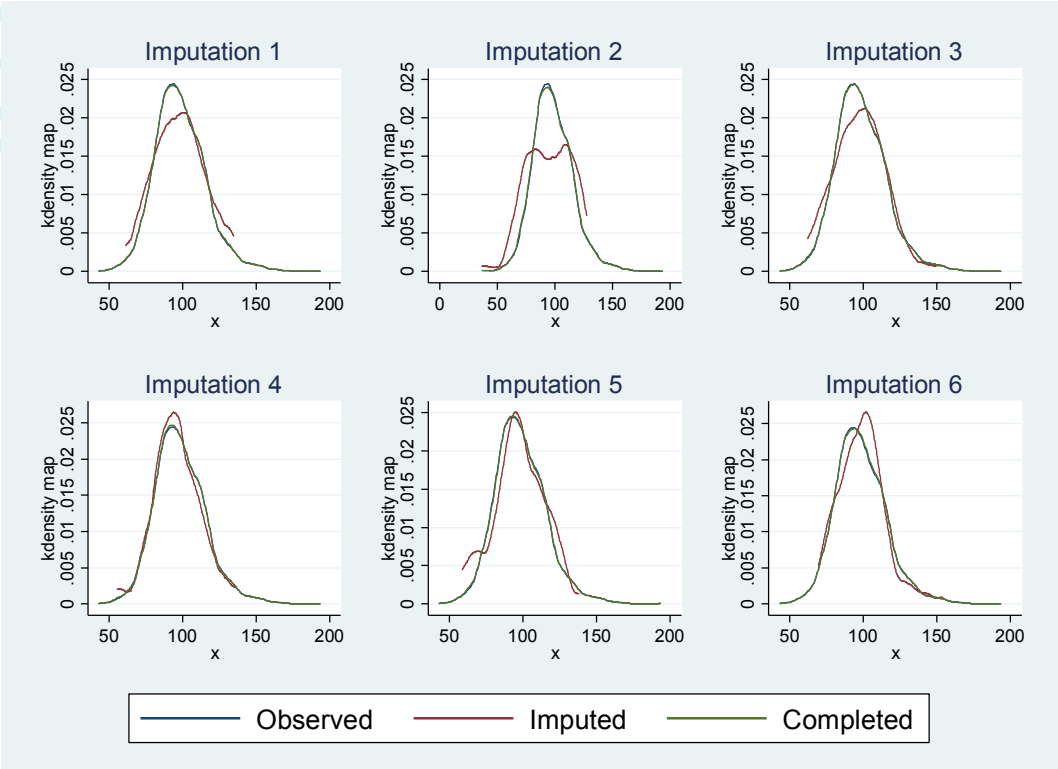
Platelets:



Charlson Score:



MAP:



Intoxication:

	Imputation 1	Imputation 2	Imputation 3	Imputation 4	Imputation 5	Imputation 6
Observed	29.7%	29.7%	29.7%	29.7%	29.7%	29.7%
Imputed	42.1%	34.2%	34.2%	39.5%	47.4%	36.8%
Completed	30%	29.8%	29.8%	30%	30.1%	29.9%

Prehospital or ED Seizure:

	Imputation 1	Imputation 2	Imputation 3	Imputation 4	Imputation 5	Imputation 6
Observed	4.4%	4.4%	4.4%	4.4%	4.4%	4.4%
Imputed	0%	22.3%	0%	11.1%	0%	11.1%
Completed	4.4%	4.5%	4.4%	4.4%	4.4%	4.4%

Prehospital or ED Vomiting:

	Imputation 1	Imputation 2	Imputation 3	Imputation 4	Imputation 5	Imputation 6
Observed	18.4%	18.4%	18.4%	18.4%	18.4%	18.4%
Imputed	8.3%	16.7%	16.7%	16.7%	33.3%	25%
Completed	18.3%	18.4%	18.4%	18.4%	18.5%	18.4%

GCS:

GCS:15	Imputation 1	Imputation 2	Imputation 3	Imputation 4	Imputation 5	Imputation 6

Observed	57.6%	57.6%	57.6%	57.6%	57.6%	57.6%
Imputed	60%	40%	60%	60%	80%	40%
Completed	57.6%	57.6%	57.6%	57.6%	57.6%	57.6%
GCS:14	Imputation 4	Imputation 2	Imputation 4	Imputation 4	Imputation 5	Imputation 6
Observed	31.5%	31.5%	31.5%	31.5%	31.5%	31.5%
Imputed	40%	40%	40%	40%	20%	60%
Completed	31.5%	31.5%	31.5%	31.5%	31.5%	31.5%
GCS:13	Imputation 4	Imputation 2	Imputation 4	Imputation 4	Imputation 5	Imputation 6
Observed	10.9%	10.9%	10.9%	10.9%	10.9%	10.9%
Imputed	0%	20%	0%	0%	0%	0%
Completed	10.9%	10.9%	10.9%	10.0%	10.9%	10.0%

Abnormal First Neurological Examination:

	Imputation 1	Imputation 2	Imputation 3	Imputation 4	Imputation 5	Imputation 6
Observed	14.5%	14.5%	14.5%	14.5%	14.5%	14.5%
Imputed	14.6%	30.3%	21.3%	21.3%	19.1%	13.5%
Completed	14.5%	15.3%	14.8%	14.8%	14.7%	14.4%

Frailty (no missing data under 50 category):

Under 50	Imputation 1	Imputation 2	Imputation 3	Imputation 4	Imputation 5	Imputation 6
Observed	38.8%	38.8%	38.8%	38.8%	38.8%	38.8%
Imputed	10.7%	7.1%	7.1%	7.1%	10.7%	10.7%
Completed	38.4%	38.3%	38.3%	38.3%	38.4%	38.4%
CFS 1-3	Imputation 1	Imputation 2	Imputation 3	Imputation 4	Imputation 5	Imputation 6
Observed	38.4%	38.4%	38.4%	38.4%	38.4%	38.4%
Imputed	64.3%	75%	75%	75%	67.9%	64.3%
Completed	38.8%	39%	39%	39%	38.9%	38.8%
CFS 3-6	Imputation 1	Imputation 2	Imputation 3	Imputation 4	Imputation 5	Imputation 6
Observed	18.4%	18.4%	18.4%	18.4%	18.4%	18.4%
Imputed	17.9%	14.3%	14.3%	17.9%	17.9%	17.9%
Completed	18.4%	18.4%	18.4%	18.4%	18.4%	18.4%
CFS 7-9	Imputation 1	Imputation 2	Imputation 3	Imputation 4	Imputation 5	Imputation 6
Observed	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%
Imputed	7.1%	3.6%	3.6%	0%	3.6%	7.1%
Completed	4.4%	4.3%	4.3%	4.2%	4.3%	4.4%

Supplementary Material 4: Multivariable Models selected in complete case analysis

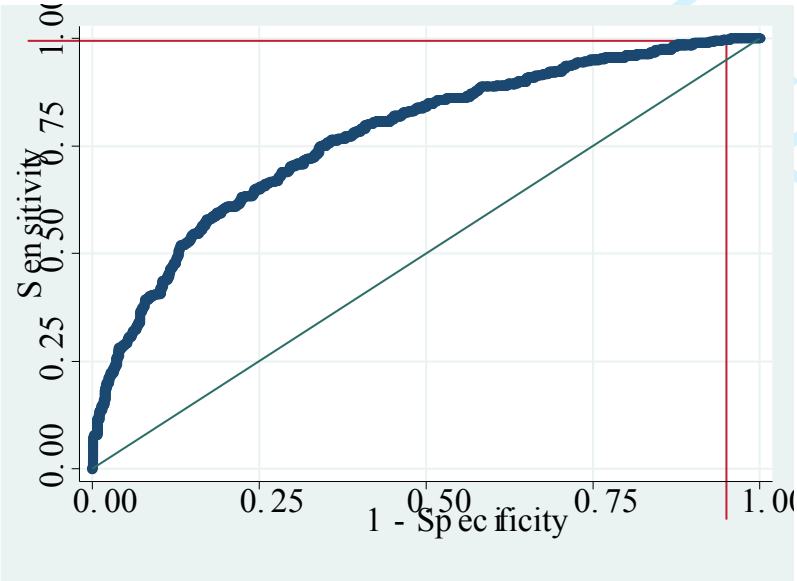
Candidate Factor	**Category**	**Multivariable effect on risk of deterioration: Odds Ratio (95% CI)**	**Multivariable effect on risk of deterioration: Odds Ratio (95% CI)**
Age	Year (1 unit increase)	*	$(Age/10)^3$ Fractional Polynomial: 0.997 (0.996 to 0.999
GCS Vs 15	GCS14 GCS13	1.5 (1.1 to 2.1) 2.7 (1.8 to 4.1)	1.6 (1 to 2.5) 4.2 (2.4 to 7.2)
Abnormal Neurological Examination	Abnormal	1.4 (0.99 to 2.1)	2.1 (1.3 to 3.5)
Injury severity on CT Vs simple skull fracture (categories described in detail supplementary material 2)	2) Complex Skull fractures 3)1-2 bleeds < 5mm (total) 4) No or minimal mass effect 5) Significant midline shift 6) High/mixed-density lesion 7) Cerebellar/Brain stem injury	1.3 (0.4 to 4.5) 0.7 (0.2 to 2.2) 1.8 (0.6 to 5.4) 5.6 (1.8 to 17.5) 14.4 (4.4 to 46.6) 10.1 (2 to 49.8)	1.3 (0.2 to 7.2) 0.6 (0.1 to 3.6) 2.3 (0.5 to 10.2) 11 (2.3 to 52) 47.4 (9.9 to 227.5) 10.5 (1.2 to 89.3)
Subdural bleed	Yes	1.8 (1.3 to 2.4)	*
Extracranial Injury	ISS (1 unit increase)	*	1.06 (1.03 to 1.1)
Rockwood Frailty Score Vs under 50	CFS 1-3 CFS 4-6 CFS 7-9	*	1.4 (0.8 to 2.6) 0.6 (0.2 to 1.7) 0.1 (0.01 to 1.05)
Preinjury Anti-coagulation or anti-platelets	Yes	1.3 (1 to 1.8)	*
Intoxicated	Yes	*	0.6 (0.4 to 0.95)

Number of Injuries on CT Vs 1	2 3 4 5 Diffuse injury	*	0.9 (0.5 to 1.5) 0.7 (0.4 to 1.4) 1.6 (0.8 to 3.1) 2.5 (1.2 to 5.1) 2.1 (0.2 to 18.4)
Contusion Present	Yes	1.3 (0.99 to 1.8)	*
Extradural bleed	Yes	1.7 (1 to 2.8)	*
Intraparenchymal haemorrhage Present	Yes	*	0.5 (0.2 to 0.9)
Intra-ventricular bleed	Yes	1.9 (0.9 to 3.9)	*

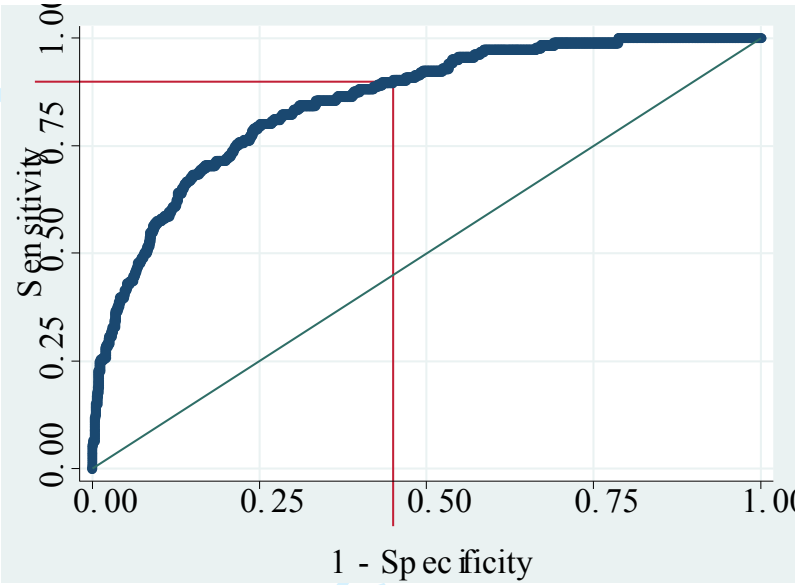
*Not Selected into model

Supplementary Material 5:

a) ROC curve of derived model for primary composite outcome of deterioration for discharge from the ED



b) ROC curve of derived model for secondary composite outcome of deterioration indicating need for specialist neurosurgical admission



*AUC estimated in patients with complete data for explanatory variables in each model

Supplementary Material 6: Performance of risk score including Hb

Factor	**Coefficient (optimism adjusted)**	**Risk Score Value**
Preinjury Anti-coagulation or anti-platelets	0.3	1
GCS 15 14 13	 0 (Vs) 0.4 0.7	 **GCS 15** 0 **GCS 14** 1 **GCS 13** 2
Normal first Neurological Examination	0.45	**Abnormal** 1.5
Number of Injuries on CT **1** **2** **3** **4** **5** **Diffuse**	 0 (Vs) 0.25 0.4 0.8 0.9 0.3	 **1** 0 **2** 1 **3** 1 **4** 3 **5** 3 **Diffuse** 1
Injury severity on CT* **1** simple skull fracture	 0 (Vs)	 **1** 0

2 complex Skull Fracture **3** 1-2 bleeds < 5mm **4** Marshall II **5** Marshall II/IV **6** Marshall VI **7** Brain stem/Cerebellar	0.3 0.08 0.7 1.7 2.7 1.7	**2** 1 **3** 0 **4** 2 **5** 5 **6** 9 **7** 5
ISS (body regions excluding head)	0.2	**Up to 2 non-significant extra-cranial injuries**** 0 **Any significant extra-cranial injury or 3 or more injuries** 2
Hb	-0.01	**Hb<10** 2
Constant	-1.38	

N=1370	**Deteriorated**	**Didn't deteriorate**	**Positive Predictive Value (PPV)** **Negative Predictive Value (NPV)**
Performance of Risk score			
Admission (Score>0)	396	912	PPV=30.3%
Discharge (Score=≤0)	2	60	NPV=96.8%
	Sensitivity = 99.5% (95% CI: 98% to 99.9%)	Specificity= 6.2% (95% CI: 4.8% to 7.9%)	

Supplementary material 7: risk stratification by risk score

Risk Score	**0**	**1-5**	**>5**
Deteriorated	2	181	242
Did not deteriorate	85	855	204
Prevalence deterioration	2.3%	15.5%	54%